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New PillHaler® device with higher resistance for dry powder formulations

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INTRODUCTION

Dry powder inhalers (DPIs) represent one of the central tools for respiratory disease therapies. Their performance, in terms of powder deagglomeration, depends on the inspiratory flow generated by the patient and on the turbulence in the device that is determined by its design and resistance parameters (Figure 1) [1-4].

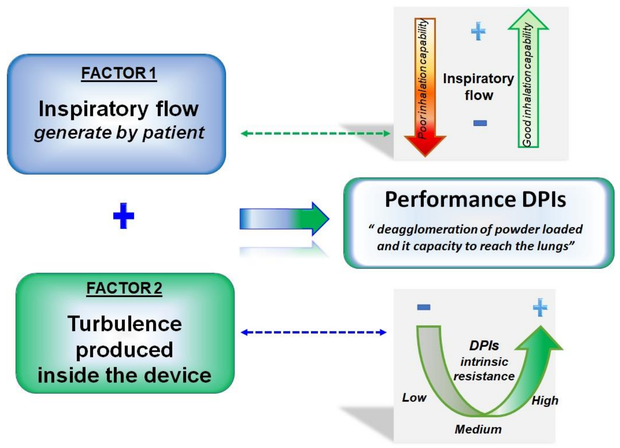


Figure 1: Factors that influencing the DPIs performance

The **PillHaler®** (Figure2A) is a disposable, single-dose (blister) and low-resistance device for DPI formulations [5].

The simple design (Figure 2B) and blister filling volume capacity allows the PillHaler® to be used with different formulations and dosages of inhalable dry powder.

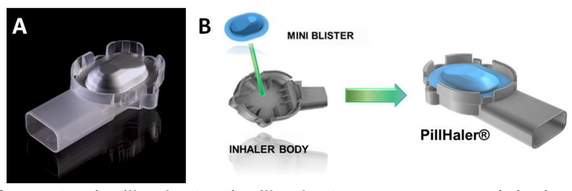


Figure 2: A) PillHaler®, B) PillHaler®: component and design

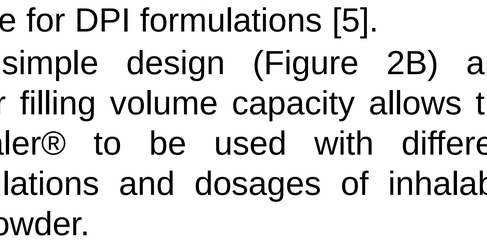
However, its application is limited for formulations that require higher inspiratory flow for powder deagglomeration, for instance for patients with a disease-induced airflow limitation that cannot achieve such inspiratory performance [6].

To overcome this problem a new prototype of the PillHaler with higher resistance has been designed.

This study aimed to assess the intrinsic resistance of the new DPI prototype and its *in vitro* aerosol performances, using a model formulation blend.

MATERIALS AND METHODS

New Prototype of PillHaler® 3D printed



PillHaler ® new prototype 3D printed

INTRINSIC RESISTANCE MEASUREMENTS

Flows measurements set up and P1 measurement

Model Formulation Blend

Component	% w/w
Fluticasone Propionate	2.5
Respitose SV003	97.5

Mixing condition
20 rpm x 90 min

Content Uniformity

Particle Size Distribution

Particle morphology
Scanning Electron Microscopy (SEM)

In vitro aerosol performance of DPIs PillHaler®

Test condition	Device	TEST SET UP Flow (L/min)	TEST SET UP *Actuation (sec)*
Different flows rate	PillHaler®	30	8
		60	4
	PillHaler® New Prototype	30	8
		60	4
2KPa	PillHaler®	90*	2.7
	PillHaler® New Prototype	41*	5.9

*Flow measured

RESULTS AND DISCUSSION

The new PillHaler® prototype differs from the original by having a different internal grid (Figure 3).

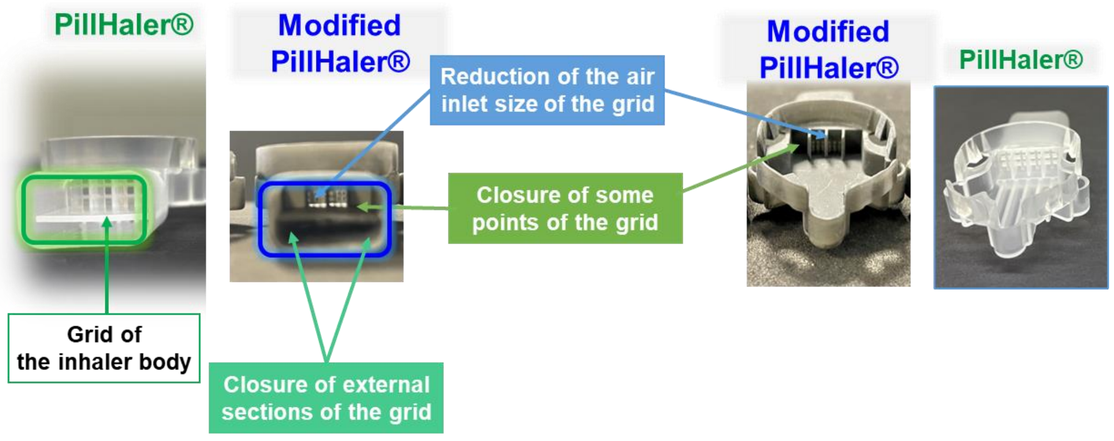


Figure 3: Grid modification in the new PillHaler® prototype

RESULTS AND DISCUSSION

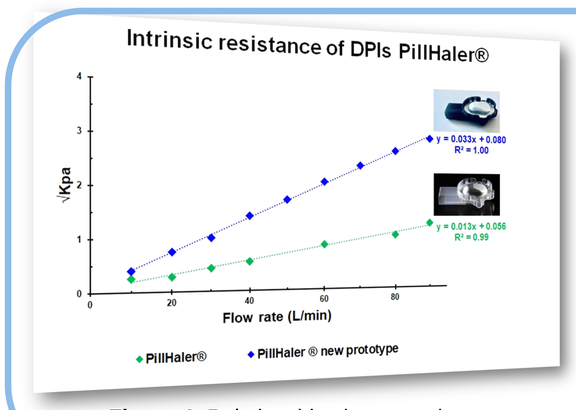


Figure 4: Relationships between the square root of pressure drop measured at different flow rates

Intrinsic resistance of the New PillHaler® Prototype

The new PillHaler present an internal resistance of 0.033 √KPa/(L/min) higher compared to the PillHaler® (0.013 √KPa/(L/min)) (Figure 4).

Model formulation blend: Characterization

- **Content uniformity:**100.8±8.3%.
- **SEM** images: lactose as carrier reduces the API agglomeration (Figure 5 A-B).
- **Particle size distribution** of the blend can be largely attributed to the carrier in the formulation (figure 5C).

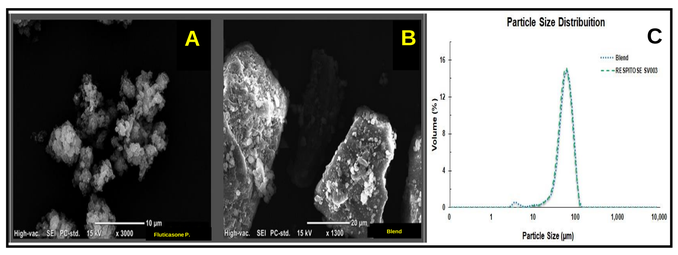


Figure 5: SEM images of A) API - B) blend and C) PSD of blend and lactose

In vitro aerosol performance of DPIs PillHaler ®

Different flows rate

- Fine particle Fraction (FPF%) of the prototype was significantly higher than the FPF% from the original PillHaler® at both flow rates tested ($p<0.05$) (Figure 6).
- No significant differences were observed for the prototype FPF% at the two flow rate tested
- The MMAD of the two different flow rates tested showed a significant difference between the PillHaler® and its prototype ($p<0.05$).

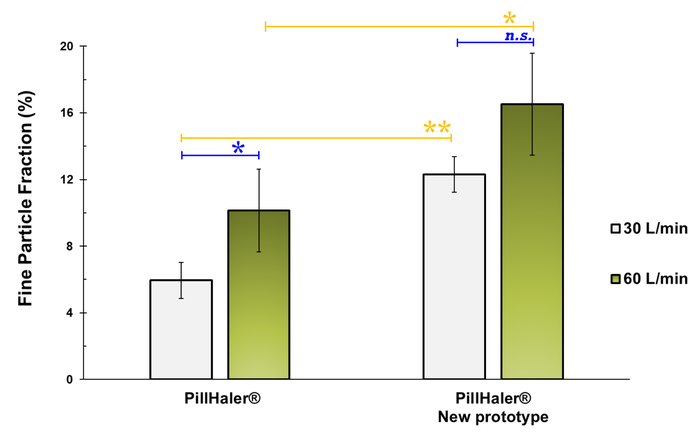


Figure 6: FPF%values at 30 L/min and 60 L/min for the PillHaler® and its new prototype with higher resistance.

2KPa

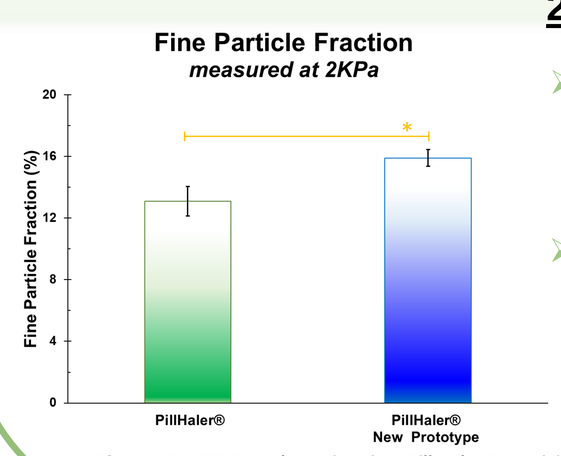


Figure 7: FPF%values for the PillHaler® and its new prototype with higher resistance.

- FPF% of the prototype was significantly higher than data obtained using the original PillHaler® ($p<0.05$) (Figure 7).
- The MMAD of the two different flow rates tested showed a significant difference between the PillHaler® and the prototype ($p<0.05$).

CONCLUSIONS

The new PillHaler® with a higher resistance has been shown to improve the aerosol deposition of a model inhalable dry powder formulation at both flow rates of 30 and 60 L/min. This was also confirmed by the data obtained at the 2 KPa of pressure drop.

The increase of the fine particle fraction parameter could be attributed to the higher resistance of the device that improves the deagglomeration of the API from the lactose carrier. Moreover, this DPI prototype has demonstrated to be able to perform efficiently at low flow rate settings.

Studies are needed to investigate this device at higher flow rates and with different types of DPI formulations.

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